A CLINICO-HISTOPATHOLOGICAL STUDY OF100 CASES OF LICHEN PLANUS

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CERTIFICATE

Certified that this dissertation entitled ***"A CLINICO-HISTOPATHOLOGICAL STUDY OF 100 CASES OF LICHEN PLANUS"*** is a bonafide work done by **DR.P.S.S. RANUGHA,** Post Graduate Student of the department of Dermatology, Venereology and Leprosy, Madras Medical College, Chennai – 600 003, during the academic year 2005 – 2008. This work has not previously formed the basis for the award of any degree.

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CONTENTS

INTRODUCTION

Lichen Planus is one of the most itchy dermatoses, worldwide in distribution, without racial, climatic or sex predilection. It is relatively common disease of the skin, also affecting the mucous membranes, nails & hair.

Lichen planus produces intolerable itching which may interfere with sleep. The cosmetically unacceptable hyperpigmentation and the hypertrophic lesions produced in the course of the disease, make it a troublesome one.

The natural course of the disease without treatment is usually prolonged. Its chronicity is associated with certain morphological types. Spontaneous resolution is not invariable and sometimes, the damage produced is permanent.

It is considered a cell-mediated reaction to some unknown antigen and various modalities of treatment are available .

REVIEW OF LITERATURE

DEFINITION

Lichen planus is a distinctive cutaneous entity with prototypic lichenoid papules that show distinctive colour, morphology and microscopic features, develop in typical locations and manifest characteristic patterns of evolution.

TERMINOLOGY

The appearance of lichen planus (Greek leichen ‘tree moss’, Latin planus ‘flat’) & lichenoid dermatoses has been likened to the scurfy, finely furrowed, dry excrescences of the symbiotic vegetation known as lichen.

The term ‘lichenoid’ is used by clinicians to describe a flat topped, shiny, papular eruption resembling lichen planus or by histopathologists to describe a type of tissue reaction consisting principally of basal cell liquefaction and a band-like inflammatory infiltrate in the papillary dermis[2].

Lichenoid eruptions occur due to drugs, contact with colour developers and in infection with Treponema pallidum[3].

HISTORICAL ASPECTS

1. William James Erasmus Wilson in 1869 delineated and named the condition lichen planus[4].
2. Hebra had described it earlier as lichen ruber planus.
3. 1895 – Wickham described the characteristic striae[5]
4. 1909 – Darrier elaborated the histopathological findings
5. 1919 – Graham little reported scalp and follicular involvement
6. 1973 – Pinkus defined lichenoid tissue reaction[2].

AETIOPATHOGENESIS

It is evident that immunological mechanisms almost certainly mediate the development of lichen planus[6]. No consistent alterations in immunoglobulins have been shown in lichen planus and humoral immunity is most likely a secondary response in immunopathogenesis.

Cell mediated immunity plays a major role in triggering clinical expression of the disease. Both $CD4^+$ & CD8+ T cells are found in lesional skin in dermis while CD8 + T cells infiltrate epidermis.

Progression of disease leads to preferential accumulation of CD8 + T cells. The CD8+ cells & CD45 + RO cells are responsible for the development of apoptosis in LP.

The epithelial lymphocyte interaction can be divided into 3 stages

1. LICHEN PLANUS – SPECIFIC ANTIGENIC RECOGNITION
2. CYTOTOXIC LYMPHOCYTE ACTIVATION
3. KERATINOCYTE APOPTOSIS

1. LICHEN PLANUS SPECIFIC ANTIGENIC RECOGNITION

a. CD8+ lesional T cells recognize an LP - specific Antigen which is presented by Langerhans cells or epidermal keratinocytes in association with MHC class I molecules. CDla+ Langerhans cells & factor XIIIa+ cells are increased in LP9.

b. The nature of antigen is unknown

c. Antigen could be an

   i) Autoreactive peptide

   ii) Exogenous Ag – altered protein / drug / contact allergen / viral or infectious agent

   iii) unidentified immunogenic target

Low grade chronic exposure to mercury, gold etc may stimulate a lymphocyte reaction that manifests as lichen planus.

The role of infection though provocative, no conclusive evidence has linked LP to infections like HCV,[10,23,24] syphilis, HSV type 2, HIV amoebiasis[11], chronic bladder infections, H.Pylori[12] , HPV, HBV infections[13] & vaccination[14].

2. CYTOTOXIC LYMPHOCYTE ACTIVATION

a) The CD8+ T cells undergo clonal expansion in tissues.

b) Production of IL-2,, IL-4, IL-10, IFNγ TNF-α & TGF-β by T lymphocytes.

IFNγ upregulates MHC class II expression & expression of ICAM-1 and VCAM-1 by basal keratinocytes, Langerhans cells, thus enhancing their interactions with lymphocytes

c) Keratinocytes produces cytokines like IL-1β, IL-4, IL-6, GM-CSF and TNF - α17.

d) RANTES19 (Regulated upon activation normal T-cell expressed and secreted) secreted by T cells may trigger mast cell degranulation with consequent release of TNF-α which

in turn up regulates lesional T-cell13 RANTES & MMP – 9 secretion.

e) Mast cell degranulation and T-cell secretion of MMP-920 may contribute to basement membrane disruption, enabling T cell migration into epidermis.

3. KERATINOCYTE APOPTOSIS

Possible mechanisms[21] include

a) T-cell secreted TNF-α binding to TNF-α R1 receptor on keratinocyte surface.

b) T-cell surface CD95L (fas ligand) binding CD95 (fas) on keratinocyte.

c) T-cell secreted matrix metalloproteinase-9 (MMP-9) disrupts epithelial basement membrane blocking cell survival signals to keratinocytes. All these mechanisms can activate keratinocyte caspase cascade resulting in apoptosis.

GENETICS

Fewer than 100 cases of familial LP[25] have been reported.

LP has also been reported in monozygotic twins[26]. Familial forms tend to be more protracted and severe and present in erosive, linear or ulcerative patterns or with atypical features affecting young adults and children.

HLA[27] haplotypes associated with familial LP – HLA B7, HLAB18, HLACW8.

HLA haplotypes[28] associated with non-familial LP – HLA A3, -A5, -A28, - B8, - B16, - BW35

HLA B8-common with oral LP as sole manifestation

HLABW35 – strongly associated with cutaneous

EPIDEMIOLOGY

Age Incidence

In India lichen planus is more prevalent in the age group of 20-40 yrs, [29,30,31] while in the west, it is more prevalent between 30-60 yrs, Both oral & cutaneous lichen planus have rarely been reported in childhood[32].

Sex Incidence

Although there is no particular sexual predilection, some studies have indicated a male preponderance[30] and few others, a female preponderance[31].

GEOGRAPHICAL INCIDENCE

Worldwide in distribution No overt racial predisposition.

An incidence of 0.38% of dermatology outpatients has been reported from a study in India.[33]

CLINIAL FEATURES

Lichen planus is characterized by shiny, violaceous, flat topped polygonal papules which retain the skin lines and which vary in size from pinpoint to a centimetre or more across, they may be closely aggregated or widely dispersed.

WICKHAM'S STRIAE[34]

Fine whitish puncta or reticulate networks, considered to be highly characteristic, more easily observed after applying oil, xylene or water and visualising the lesions with a magnifying lens or a handheld dermatoscope. It is due to localized thickening of stratum granulosum although a focal increase in the activity of lichen planus may account for it.

KOEBNERIZATION

In the acute, evolving stage of the disease, scratching, injury or trauma may induce an isomorphic response[37].

According to Brocq, methodical grattage produces turgescence of papules and eventually subepidermal purpura.

SITES AFFECTED

LP can affect any part of the body, but the extremities are involved usually symmetrically.

The volar aspect of wrist, flexural areas of arms, legs, lumbar region, around the ankles are often involved. Lower limbs have been found to be most commonly involved in many Indian studies[29]. (Pillsburyetal, 1956; Ormbsby & Montgomery, 1954; Sutton, 1956).

The ankles and shins are the commonest sites for hypertrophic lesions. Face is usually spared and palmoplantar involvement is unusual. Inverse lichen planus affects axillae, groin and inframammary areas. All the mucosal sites may be affected.

NATURAL HISTORY & EVOLUTION

Although a few cases evolve rapidly and clear within a few weeks, the onset is usually insidious. In most cases, the papules eventually flatten over a few months, often to be replaced by an area of pigmentation that retains the shape of the papule & persists for months or years.

In a third of cases, further spread of lesions occurs. In generalized disease, the eruption often spreads within 1-4 months from onset.

One Indian study reported the duration to be from 1 month to 7 years[33.] (Bhattacharya M etal).

Another Indian study has found the duration to vary from 5 days to 30 yrs (Kachwa D et al).

In the majority of patients the average duration is about 15 months. Oral & hypertrophic lesions tend to have a chronic course. Relapse occurs in less than 20% patients[36].

SYMPTOMATOLOGY

Itching is a fairly consistent feature of lichen planus[29,31]. It may vary from mild irritation to severe itching. A few cases are asymptomatic.

Hypertrophic lesions itch severely. Paradoxically, there is seldom evidence of scratching, as the patient rubs rather than scratches to gain relief.

Oral involvement can present with discomfort, stinging or pain especially on intake of hot foods and drinks. Ulcerated lesions are especially painful.

ROLE OF VARIOUS PROPOSED AETIOLOGICAL FACTORS IN LICHEN PLANUS

LP as a viral infection.; Thyresson and Moberger (1957) considered lichen planus as a skin manifestation of a dermatotropic virus. Virus-like particles had been identified in basal layer by some. But later, studies with electron microscopy by Tuffanelli in 1976 did not show any viral particles.

Several studies have analysed the association of liver disease and lichen planus. A few have reported a positive association. [40] [41], but many others have demonstrated no association[42,43]. The association of carbohydrate intolerance and frank diabetes mellitus with lichen planus has also not yet been proved beyond doubt. However, a few studies have indicated a positive association.[44,45] Grinspar etal in 1965 reported an incidence of 6% of LP in patients with carbohydrate intolerance.

Recently many studies have reported a strong association of Hepatitis B vaccination and lichen planus in children.[13,14]. The HBsAg component of vaccine might be responsible (Saywell CA etal).

The LP lesions develop on an average 40 days after vaccination[47]. (Rybojad M et al)

No well established association has been documented between emotional stress[46,] tobacco use, oral or gastrointestinal candidiasis, or carbohydrate intolerance and development of lichen planus.

CLINICAL VARIANTS

1. According to configuration of lesions
    a) Annular
    b) Linear
2. According to Morphology
    a) Hypertrophic LP
    b) Atrophic LP
    c) Vesiculobullous
    d) Erosive & ulcerative

e) Follicular

f) Actinic

g) Lichen planus pigmentosus

h) Other rare forms – perforating, guttate etc

3. According to site of involvement

a) Palms & soles

b) Mucosa

c) Nails

d) Scalp

ANNULAR LICHEN PLANUS

Arcuate groupings of individual papules that develop rings or peripheral extension of clustered papules with central clearing. They may be widely scattered and usually have a very narrow rim of activity and a depressed slightly atrophic centre (annular atrophic lichen planus) Site : More common on the penis .

Actinic LP is frequently annular. Also has predilection for intertriginous areas like axilla, groin. Annular atrophic lichen planus is

frequently chronic. The central atrophy is due to elastolysis by the infiltrating inflammatory cells.

Another form of annular lichen planus occurs when larger lesions reach 2 to 3 cm in diameter and become hyperpigmented with a raised outer rim .This may occur on the trunk or extremities.

LINEAR LICHEN PLANUS

a) Linear lesions as part of koebnerization.

b) Isolated linear lesions, made of small papules in close opposition are rare. More common in childhood.

c) Long narrow lesions along the whole length of a limb – overlap with lichenoid epidermal nevus (Bronstein MH et al, 1989)

d) Multiple linear LP along Blaschko's lines (Kabbash C et al, 2002) has been reported.

e) Multiple linear LP in a HIV patient (Ruiz Villavede R et al, 2002).

f) Segmental LP co-localized with vitiligo in a case (Sardana K et al , 2002)

g) Zosteriform LP has also been described. (Khanna N et al, 1996).

h) Lichen planus can develop at the site of healed zoster.

HYPERTROPHIC LICHEN PLANUS (LICHEN PLANUS VERRUCOSUS)

1. Usually occurs on the extremities, around the ankle, shins & interphalangeal joints.
2. Most pruritic variant
3. Lesions are thickened, elevated, purplish or reddish brown in colour & hyperkeratotic
4. Chronic course
5. Chronic venous insufficiency is frequently present
6. Heals with scarring, atrophy, hyper or hypopigmentation.
7. Multiple cutaneous horns, keratoacanthoma and malignant transformation has been reported.
8. Photodistributed hypertrophic lichen planus has been described in a patient with AIDS.

ATROPHIC LICHEN PLANUS

1. Few well demarcated white-bluish papules or plaques with central superficial atrophy.

2. Resolved hypertrophic and annular lesions present as atrophic lichen planus.

3. Usually in the lower extremities or trunk.

VESICULO BULLOUS LICHEN PLANUS

a) Development of vesicles and bullae from the papules of lichen planus and rarely from normal appearing skin

b) The eruption is only of short duration and resolves in a few months.

c) Can be differentiated from LP pemphigoides by immunofluorescence

EROSIVE & ULCERATIVE LICHEN PLANUS

a) Chronic painful bullae and ulcerations of the feet with typical lesions of nails, skin and mucosa.

b) Permanant loss of toe nails and cicatricial alopecia of the scalp are common.

c) Squamous cell carcinoma may develop.

d) Severe cases of oral lichen planus can present with erosions & ulcers extending to the posterior pharynx, larynx and rarely, even the oesophagus.

FOLLICULAR LICHEN PLANUS

a) May occur alone or in association with other forms of cutaneous or mucosal LP

b) Synonyms : lichen planus follicularis, peripilaris, acuminatus

c) Individual keratotic follicular papules and studded plaques are seen.

d) Sites affected – Trunk and medial aspect of proximal extremities.

e) Scarring alopecia of the scalp can occur

f) Variants –

1. Graham Little Piccardi Lassueur Syndrome

2. Pseudopelade of Brocq

3. LP follicularis tumidus with oval pseudotumoral plaques of mastoid area

4. Postmenopausal frontal fibrosing alopecia

g) Fountain sign – Injection of saline around follicle leads to discharge of saline through follicular orifice like fountain.

ACTINIC LICHEN PLANUS

(Lichen planus subtropicus, summer time actinic lichenoid eruption, lichenoid melanodermatosis) common in

a) Middle East ,East Africa and India

b) Common in children and teenagers[64.] Mean age – 14 yrs

c) Incidence in various Indian studies has varied from 4 to 14%

d) 3 clinical types

a) Annular – commonest

b) Pigmented – Melasma – like[65]

c) Dyschromic

e) Sites – exposed areas of face, dorsal hands, arms, nape of the neck.

f) Pruritus & scaling are minimal

LICHEN PLANUS PIGMENTOSUS

a) Slate gray to brownish black macules over sun exposed areas and occasionally over intertriginous areas[67].

b) The pigmentation may be diffuse, reticular, blotchy or perifollicular.

c) Mucosa, palms & soles are usually not involved.

d) May or may not be associated with LP papules

e) Middle East & India

OTHER RARE FORMS

1. Perforating variant – Transepidermal elimination of lichen planus like inflammatory tissue is observed

2. Exfoliative & exanthematous form.

3. Invisible de Gougerot – lesions are not perceptible with visible light but become apparent with WOOD'S LAMP examination.

4. Guttate LP – widely scattered, discrete lesions, may be small or large.

5. Acute and subacute LP with confluence of lesions – may simulate PR in the early phase and eczema later. Drug induced lichenoid eruptions may present in this fashion.

LP OF PALMS AND SOLES[68]

1. It is rare, may present diagnostic difficulty if present as an isolated finding.

2. Pruritus may or may not be present

3. Lacks the characteristic colour & shape of lesions elsewhere.

4. Inner plantar arch, lateral aspect of fingers & palms are involved.

5. Erythematous scaly plaques or yellowish[69] hyperkeratotic papules may be seen.

MUCOSAL LICHEN PLANUS

ORAL MUCOSA – lesions may be confined to the mouth or be accompanied by skin lesions & account for 15% all cases[70.]

The types of lesions include Reticular, Atrophic, Papular, Plaques, Erosive & Bullous forms.

Reticular LP is the most frequent type[71].

The lesions are bilateraal[72] & involve the lips, tongue, buccal mucosa & gingivae.

They are often symptomless but may cause soreness & pain particularly in erosive type.

GENITAL INVOLVEMENT

Males : Classical red-purple papules, patches & plaques and annular lesions can occur over penile shaft, glans, prepuce, scrotum, groins & perianal skin. Phimosis can occur. The lesions may be localized to anogenital or be part of generalized involvement. Erosive form can occur as peno-gingival syndrome[73]. Usually, anogenital LP is self-limiting.

Females : Vulval involvement[74] may occur in isolation or it may be part of generalized outbreak in 20% of cases or associated with oral involvement alone. The clinical lesions include papules, white or annular plaques and erosions with or without lacy borders. Erosive lesions may involve labia minora, clitoris & clitoral hood. Other clinical forms include pigmented &flexural LP, vulvovaginal gingival LP[75] & lichen plano pilaris of vulva.

Erosive forms can present with dyspareunia, scarring & loss of normal vulvar architecture.

Other Mucosae which can be involved are oesophagus, conjunctiva, urethra, anus, nose & larynx.

Oesophagus – dysphagia & strictures

Anus – leucokeratosis, hyperkeratosis, fissuring & erosions, conjunctiva – cicatricial conjunctivitis.

LP OF NAILS

a) Nail involvement[77] occurs in 10% of cases of widespread LP.

b) Isolated involvement is rare, often followed by clinical involvement elsewhere.

c) 5^{th} & 6^{th} decades are usually affected, long term permanent damage is rare.

d) Thinning, longitudinal ridging, linear depressions & onychoschizia are the most common findings.

e) Other findings of nail matrix involvement are onychorhexis, longitudinal melanonychia[78], leukonychia, pterygium & loss of nails

f) Nail bed involvement can lead to onycholysis & subungual hyperkeratosis

g) Bluish discoloration of proximal nail fold, yellow-nail syndrome like features can also occur

h) 'PUPTENT' SIGN – Nail bed involvement that elevates the nail plate & may cause longitudinal splitting

g) Nail involvement in childhood[76] is rare. Twenty nail dystrophy may occur as an isolated finding.

LP OF SCALP

1. Uni or multifocal areas of scarring alopecia occur.

2. Middle aged women are usually affected

3. Recent scalp lesions may show violaceous papules ,erythema and scaling .These papules are replaced quickly by follicular plugs and scarring. Eventually the plugs are shed from the scarred area which remains white ,smooth and atrophic.Follicular orifices are absent in the area of alopecia. If the patch is extending , horny plugs may still be present in follicles around its margins and the hair pull test will be positive at the margins.

4. Patients usually present with pseudopelade like patches of scarring that are non-specific.

5. Scalp may be involved alone or associated in 50% of cases with

   a. Bullous lichen planus with shedding of nails.

   b. bullous lesions with typical lichen planus lesions of skin and mucosa.

   c. Lichen planopilaris of trunk

6. The variants of cicatricial alopecia due to lichen planus are lichenplanopilaris[79], Graham Little Piccardi Lassueur syndrome, post menopausal frontal fibrosing alopecia[80]. lichen planus follicularis tumidus, lichen planoporitis and pseudopelade of Brocq.

7. Frontal fibrosing alopecia- resembles androgenetic alopecia with frontal recession ,but on close inspection, loss of follicular orifices and perifollicular erythema with hyperkeratosis at the marginal hairline.Frontal hairline recedes in a straight line rather than bitemporally.

8. Lichen planoporitis - lichenoid reaction centered over acrosyringium and eccrine ducts entering the epidermis.

9. Natural history - slow progression over many years.No effective treatment available.

INVERSE LICHEN PLANUS

Rare Red-brown discrete papules and nodules. Flexural areas like axilla, inframammary, groin are involved.

HISTOPATHOLOGY

Typical papules show the following features[81]

a. Compact orthokeratosis

b. Wedge-shaped hypergranulosis

c. Irregular acanthosis

d. Vacuolar alteration of basal layer

e. Band-like dermal lymphocytic infiltrate in close approximation to the dermis.

WICKHAM'S STRIAE

Focal increase in thickness of granular layer and infiltrate.

Rete ridges show irregular lengthening with some showing flattening & pointed ends – 'SAW TOOTHING'

Dermal papilla between retiridges – dome shaped

COLLOID BODIES[82] – Hyaline, cytoid, or civatte or Sabaurod's bodies

20μ in diameter homogenous, easinophilic PAS positive, diastase resistant.

Present in the lower epidermis and upper dermis formed by filamentous degeneration of damaged keratinocyes.

Colloid bodies are best seen with PAS stain but can be recognized with routine H&E stain. Colloid bodies occur most frequently in the early , well developed lesions and do not extend throughout the length of the section ,so should be searched for.

MAX JOSEPH SPACE[83] - Focal separation of epidermis from dermis

BAND-LIKE Inflammatory infiltrate[47] – sharply demarcated at its lower border.

Composed entirely of lymphocytes intermingled with macrophages and few eosinophils and / or plasma cells.

Pigmentary incontinence with dermal melanophages is characteristic

HYPERTROPHIC LP[84]

- Considerable acanthosis, papillomatosis, hypergranulosis and hyperkeratosis.
- Interface vacuolar changes – limited to base or rete ridges.
- Infiltrate around follicular epithelium may be present.
- Vertical streaking of collagen bundles.

ATROPHIC LP

- Thinned out epidermis, though relative compact hyperkeratosis remains
- Relatively few colloid bodies. Dermal fibrosis & loss of elastica, complete effacement of rete ridges.

FOLLICULAR LP[85]

- Band-like infiltrate around infundibulum & isthmus.
- Vacuolar changes of basal layer of outer root sheath.
- Follicular Keratin plugging

- Interfollicular epidermis often spared. In well developed lesions, perifollicular fibrosis and epithelial atrophy – hourglass configuration

MUCOSAL LP[86]

- Thinned out epidermis
- Both parakeratosis & orthokeratosis seen. Colloid bodies fewer
- Bank-like infiltrate – more of plasma cells. Ulceration may develop

LP PIGMENTOSUS

- Prominent pigment incontinence that extends deeper into reticular dermis. Less prominent inflammatory infiltrate.

BULLOUS LP

- Infrabasal blister such that there is wide separation between epidermis and infiltrate.

LP ACTINICUS

- Thinning of epidermis at the centre of lesion. More pigment incontinence in upper dermis.

TWENTY NAIL DYSTROPHY

- Typical LP involving nail matrix or
- Spongiosis prominent as in cases associated with atopic dermatitis

OLD INACTIVE LESIONS

- Reduced inflammatory infiltrate, increased melanophages

LICHEN PLANUS - LUPUS ERYTHEMATOSUS OVERLAP SYNDROME

- Histology & IF may show features of LP or lupus predominantly or both may coexist.

LICHEN PLANUS PEMPHIGOIDES[87]

- Bulla from non-lesional skin shows subepidermal bulla with eosinophilic infiltrate similar to BP.

HISTOPATHOLOGICAL DIFFERENTIAL DIAGNOSIS

- **Lichen planus like keratoses**

  Focal parakeratoses and adjacent solar lentigines in addition to typical histological picture of lichen planus Clinically , it is a solitary and non pruritic lesion.

- **Lichenoid drug eruptions**

Focal parakeratoses with concomitant absence of granular layer Necrotic keratinocytes in the basal and spinous layer. Exocytosis of lymphocytes to the upper layers of epidermis Deeper inflammatory infiltrate with numerous eosinophils.

- **Lichenoid lupus erythematosus**

  Atrophy of epidermis in addition to acanthosis. Absence of eosinophilia of keratinocytes in spinous layer. Superficial band like infiltrate with a superficial and deep perivascular and periadnexal infiltrate.

  Presence of a thickened PAS positive basement membrane . Dermal mucin deposits

Direct Immunofluorescence- Linear or granular deposits of IgG and C3 predominate in lesional skin.

In lichen planus, clusters of necrotic keratinocytes with absorbed immunoglobulins and complement are found.

Langerhans cells are decreased in DLE & SLE whereas in lichen planus , they are increased.

- **Chronic GVHD**

Inflammatory infiltrate tends to be perivascular instead of band like.

Langerhans cell number is reduced and nearly all intraepidermal lymphocytes are cytotoxic suppressor T-cells.

- **Lichen simplex chronicus**

Longstanding hypertrophic lichen planus resembles LSC , but deeper sections of hypertrophic LP may still show areas of damage to the basal layer at the base of rete ridges.

- **Early SCC in situ**

Both oral LP and SCC in situ may show hyperkeratosis and inflammatory infiltrate close to the epidermis.

But SCC in situ shows more atypical cells.

- **DLE**

LPP of scalp in early phase resembles DLE.

DLE affects hair follicles as well as interfollicular epidermis.

DLE shows vacuolar degeneration of basal cells both in epidermis and in the hair follicles without disappearance of basal cells.It also shows a thickened basement membrane and interfollicular, superficial and deep perivascular infiltrate.

ELECRON MICROSCOPY

Basal Keratinocytes together with their desmosomes and hemidesmosomes show degenerative changes. Necrotic keratinocytes[88] often still contain cell organelles (Melanosomes and Mitochondria) but only rarely contain nuclear material.

The dermal infiltrate causes damage to the lamina densa (fragmentation) followed by reduplication & irregular folding. Some of

the lymphocytes have hyperconvoluted nuclei & appear indistinguishable from Sezary cells.

IMMUNOFLUORESCENCE

Necrotic keratinocytes identified by IgM staining. IgG, IgA, C3 & fibrin[89] may be also found. They are found in large numbers or arranged in clusters. Shaggy deposition of fibrinogen at DEJ.

LPP – IgM and / or IgA, & rarely C3 at the level of infundibulum and isthmus. Shaggy deposition of fibrinogen around affected follicles. DEJ – negative for immunoreactants.

LP Pemphigoides - IgG & C3 deposited linearly along the BMZ. C3 is localized to lamina lucida as in bullous pemphigoid

IMMUNOHISTOCHEMISTRY

- Infiltrating cells are predominantly T- lymphocytes with very few B lymphocytes.
- More than 90% are activated T- lymphocytes expressing HLA-DR antigen and IL-2 receptor.
- Both CD-4 + T-lymphocytes and CD-8 + T-lymphocytes participate in the immunological reaction .

- Immunophenotyping studies on T- lymphocytes have shown that the majority of clones were CD-8 + T- lymphocytes which displayed suppressor activity and expressed αβ-T cell receptor.

- In the epidermis ,adjacent to the infiltrate ,basal keratinocytes express HLA-DR surface antigens and ICAM-1 ,both of which are implicated to enhance the interaction between lymphocytes and their epidermal targets resulting in keratinocyte destruction.

- Langerhans cells are increased in the epidermis very early in the disease.

ASSOCIATED CONDITIONS

Auoimmune Disorders

Alopecia areata, Vitiligo, Diabetes Mellitus, Morphoea, Lichen sclerosus, SLE, Dermatomyositis, Pemphigus, Myasthenia gravis, Primary biliary cirrhosis, Primary sclerosing cholangitis Autoimmune chronic active hepatitis, Ulcerative colitis.

Malignancies

Bullous LP may be[55] associated with lymphosarcoma, Castleman's tumour, Carcinoma of stomach, Craniopharyngioma and Thymoma. Paraneoplastic lichen planus of skin & mucosa may be associated with cicatricial conjunctivitis.

SYNDROMES ASSOCIATED WITH LICHEN PLANUS

1. Graham Little Piccardi Lassueur[90] Syndrome

Patchy cicatricial alopecia of the scalp, patches of follicular spinous papules involving the trunk and patches of non-cicatricial alopecia in axilla and pubic area.

2. Grinspan's Syndrome[91]

Association of oral lichen planus with vascular hypertension and diabetes mellitus.

3. Jolly's Syndrome

Association or oral lichen planus with diabetes mellitus

4. Lichen Planus / Lupus Erythematosus Overlap Syndrome

Features of reticular white lesions in oral cavity, lichenoid lesions with chronic atrophic disseminated lupus erythematosus like lesions on

the head, neck and upper trunk. Extensive generalized lichen planus can be associated with subacute cutaneous disseminated lupus erythematosus.

5. Vulvovaginal Gingival Syndrome Of Hewitt & Pelisse

Desquamative vaginitis and gingivitis

COMPLICATIONS

a) Cicatricial alopecia

b) permanant loss of nail – especially the variant with ulceration of soles

c) Ulcerative, atrophic and plaque type of oral lichen planus, vulval lesions and hypertrophic lesions of skin have the potential of developing into squamous cell carcinoma.

d) Cicatricial conjunctivitis and lacrimal canalicular obstruction.

DIAGNOSIS

The appearance of the typical papule of lichen planus is usually sufficient to make the correct diagnosis. No specific abnormalities of laboratory analyses are seen in lichen planus. Histopathological and

immunofluorescent evaluation will confirm the diagnosis in cases presenting with atypical lesions.

DIFFERENTIAL DIAGNOSIS

a. Linear LP

From nevus unis lateris, lichen striatus, linear psoriasis.

b. Annular LP

Granuloma annulare-no scales or Wickham striae in granuloma annulare.

c. Hypertrophic LP –

From lichen simplex chronicus, papular lichen amyloidosis and prurigo nodularis.

d. Atrophic LP

From lichen sclerosus et atrophicus or guttate morphoea.

e. LP pigmentosus

From erythema dyschromicum perstans.

f. Follicular LP

May resemble lichen nitidus & lichen spinulosus

g. Cicatrical alopecia due to LP

From other causes of cicatricial alopecia like lupus erythematosus, cicatricial pemphigoid.

h. Vesiculobullous LP

From LP pemphigoides by direct and indirect immunofluorescence

i. Guttate LP

From guttate psoriasis

j. Palmoplantar LP

May resemble Psoriasis vulgaris, warts, calluses, porokeratoses, hyperkeratotic eczema, tinea or secondary syphilis.

k. Lesions of tongue & buccal mucosa

From leukoplakia. Gum margin lesions from gingivitis or chronic candidiasis. Palatal lesions from smoker's patches, white sponge nevus.

l. Lesions of female genitalia

From lichen-sclerosus or leukoplakia.

m. Twenty nail dystrophy can be caused by psoriasis and alopecia areata other than LP.

n. Lichenoid eruptions are lichen planus like eruptions produced by GVHD, drugs and exposure to colour film developers. They are differentiated by absence of oral lesions, psonasiform morphology, more itching, positive patch test to offending chemicals. Histologically they are differentiated by foci of parakeratosis, more of eosinophilic infiltrate and colloid bodies higher up in the epidermis.

TREATMENT

CUTANEOUS LP

a) Topical Steroids

Potent – 0.05 % fluocinolone acetonide , 0.05 % clobetasol propionate.

Under occlusion for localized and hypertrophic lichen planus

b) Intralesional Steroids

Triamcinolone acetonide – for oral , cutaneous and nail LP. 5 to 10 mg \ml injection given every 4 weeks.Improvement in 3 to 4 months. Monitor for atrophy or hypopigmentation

c) Systemic Steroids

Prednisolone 30 to 80 mg per day for 4 to 6 weeks and then gradual tapering.

LPP-oral steroids for 3 months.

Long term chronic continuation of oral or injected steroids is contraindicated.

d) Oral Retinoids

Tretinoin – 10 to 30 mg per day

Acitretin – 30 mg per day

e) ***Puva***

For generalized LP

Both oral and topical PUVA can be used.

f) Immunosuppressants

Cyclosporine – 3 to 10 mg \kg \day-for recalcitrant cases and ulcerative LP

Azathioprine

Mycophenolate mofetil

g) Other Drugs

1. Dapsone
2. Antimalarials
3. Thalidomide
4. Oral metronidazole

5. LMW Heparin

6. Cyclophosphamide, Methotrexate, Phenytoin, Levamisole

ORAL LP

Good oral hygiene, replacement of amalgam with composite material

1. Topical, intralesional and systemic steroids
2. Topical Lidocaine gel or diphenhydramine to alleviate discomfort
3. Vaginal or rectal suppositories of steroids
4. Topical tretinoin or isotretinoin gel
5. Oral retinoids [94]
6. Topical cyclosporine
7. Topical tacrolimus and pimecrolimus
8. Oral cyclosporine[95]
9. Others – Griseofulvin, itraconazole, hydroxychloroquine, thalidomide etc can be tried.

Malignant transformation of LP lesions can be treated with surgery and radiotherapy.

LICHEN PLANOPILARIS

a. Short course of systemic steroids

b. Intralesional and topical steroids

c. Hydroxychloroquine

d. Acitretin

COURSE & PROGANOSIS

85% lesions clear within 18 months. Mean duration of oral LP is 5 yrs. The duration of disease is in the following order.

Generalised < Cutaneous < Cutaneous + mucous membrane

< mucosal < hypertrophic = lichen planopilaris

Relapse occurs in 15-20% cases[71]. Lichen planopilaris is the most chronic. Reticular oral LP has better prognosis than erosive disease. Itching disappears first, the papules flatten to be replaced by a corresponding area of post-inflammatory hyperpigmentation.

Malignant transformation may occur in < 1% of persistent oral mucosal lesions on long term follow up & still rarely in hypertrophic LP or ulcerative LP of sole offeet.

AIMS OF THE STUDY

1. To study the age and sex incidence of lichen planus
2. To study the incidence of various clinical types of LP
3. To study the main symptomatology and various sites of distribution of lesions.
4. To study the histopathological features
5. To look for any known provocative factors by relevant history and investigations.
6. To look for associated disorders if any .

MATERIALS AND METHODS

100 patients of lichen planus were selected at random from the outpatients of Department of Dermatology, Madras Medical College during the period from April 2006 to April 2007. The cases were examined thoroughly Diagnosis was made by history, clinical examination & histopathological features.

PROCEDURE

History

Enquiries were made with regard to symptoms, their duration, history of taking any drugs prior to lesion development and nature of occupation of the patient. Detailed personal history regarding other skin diseases, personal habits, exposure to STDs and possibility of emotional or physical stress prior to the onset of lesions was recorded. History of Diabetes mellitus and hypertension were asked for. Family History of similar skin lesions was enquired. History of remissions and exacerbations with or without treatment was noted.

CLINICAL EXAMINATION

Patients were examined under good day light and with a magnifying lens. The sites affected, types of changes in skin, mucous membranes and nails along with other associated disorders if any were made note of. General and systemic examination was done in all cases. Opinion regarding ENT & dental sepsis was sought from the relevant departments of Madras Medical College.

EXCLUSION CRITERIA

1) Lichenoid eruptions

2) Patients already under treatment, outside or at our hospital, irrespective of whether this was the first episode or recurrence.

LABORATORY INVESTIGATIONS

Routine hematological investigation was done in all cases. Blood sugar, liver function test, Hepatitis B surface Antigen & Serology for STD was done in all cases. Urine & Motion examination was also done for all cases.

Biopsy of skin lesions was done, (the specimen preserved in 10% formalin) and sent for histopathological examination. Specimens were studied with H & E stains.

Clinical photos were taken prior to commencement of investigations and treatment.

OBSERVATION

1. AGE INCIDENCE

The age incidence in the study group was as follows

Age in Yrs	*No. of Cases*
0-9	3
10-19	17
20-29	11
30-39	30
40-49	15
50-59	21
60-69	2
70-79	1

The youngest case was 2 yrs old and the oldest 78 yrs old.

2. SEX INCIDENCE

Of the 100 cases, 55 were female & 45 male. No positive family history was found in any of the cases

Sex	*No. of Cases*
Male	45
Female	55

The main duration varied from 1 week to 4 yrs. History of recurrence was found in 5 cases.

4. SYMPTOMATOLOGY

Symptomatology	*No. Of Cases*
Itching (moderate to intense)	95
Burning sensation on taking hot foods	25

Itching was the predominant symptom in 95 cases excluding the cases with isolated mucosal or nail involvement. The severity of itching varied from moderate to intense. All the hypertrophic lesions were very itchy.All patients with oral mucosal involvement complained of burning sensation over the lesions on taking food.

5. CLINICAL TYPES

Clinical Type	*No. of Cases*
Classical	68
Hypertrophic	12
Linear	6
Follicular	4
Annular	3
LP Pigmentosus	2

Clinical Type	*No. of Cases*
Oral Mucosa Alone	3
Actinic	2
Total	100

- Oral mucosal involvement as the sole manifestation was seen in 3 cases. However, oral involvement associated with skin lesions was seen in 22 cases.
- So, oral mucosa was involved in 25 cases.
- Nail involvement was found in 10 cases.
- Koebnerization was seen in 30 cases.

6. ORAL INVOLVEMENT

Oral Mucosal Involvement	*No. of Cases*
Oral involvement alone	3
Oral involvement with skin lesions	22

7. MORPHOLOGY & SITES OF DISTRIBUTION

1. Lower limb was the predominant initial site of involvement seen in 60 cases. Papules and plaques were the commonest lesions seen.

2. Lesions were bilaterally symmetrical in most of the cases.

3. Axilla & groin were involved predominantly in 3 cases although a few lesions were seen at classical sites.

4. 25 cases showed generalized cutaneous involvement

5. A few cases of generalized cutaneous involvement started as guttate lesions over trunk which gradually transformed into classical papules and plaques.

6. 2 cases showed hyperpigmented patches & plaques surrounded by hypopigmented or violaceous ring in children

7. **HYPERTROPHIC LP** – Pigmented nodules & violaceous plaques were seen over both shins and ankles, some showing central atrophy and depigmentation. No malignant transformation was seen in any of the lesions.

8. **LINEAR LP** – of the 6 cases, 3 showed linear unilateral lesions along either upper limb or lower limb. 2 cases had zosteriform lesions, one over thoracic & other over lumbar dermatome.

   A 2 yr old female child had multiple linear LP lesions.

9. **FOLLICULAR LP** - Of the 4 cases seen, 3 had cicatricial alopecia with one having cutaneous findings in addition. One

case showed follicular papules over trunk with no involvement of scalp.

10. **ANNULAR LP -** All the three annular LP cases had isolated annular plaques over penis with no cutaneous or mucosal involvement

11. **LP PIGMENTOSUS** - Diffuse pigmented macules were seen symmetrically over the sun-exposed areas .

12. **ORAL MUCOSA -** The sites involved were buccal mucosa, tongue, gums, palate & lips.

    The various types of lesions seen were violaceous papules, pigmented patches & plaques, reticulate networks.

    Tongue showed whitish plaques over dorsum and sides. Isolated lip involvement with skin lesions without involvement of oral mucosa was seen in a case.

13. **GENITAL INVOLVEMENT** - Violaceous papules and plaques were seen over pubic area, groin and labia majora as part of generalized cutaneous involvement.

14. **ACTINIC LP** - Annular plaques were seen over forehead, temples, dorsum of hands.

15. **PALMOPLANTAR INVOLVEMENT -** Usually occurs with cutaneous involvement. Grouped violaceous papules[2] plaques, pigmented scaly plaques, yellowish plaques & fissuring were the different types of lesions seen.

    Central aspect of palms & instep of soles were the most common sites involved with a few papules over adjoining wrist or ankle

16. NAILS - The commonest nail changes seen were longitudinal ridging followed by longitudinal melanonychia. Pterygium was seen in 1 case.

8. HISTOPATHOLOGY

Histopathological Finding	***No of Cases***
Hyperkeratosis	95
Focal Hypergranulosis	85
Basal cell degeneration	100
Pigment incontinence	100
Band like inflammatory Infiltrate	90
Saw-Toothing of Rete Ridges	80
Colloid Bodies	40

1. Hyperkeratosis was observed in 95 cases and focal hypergranulosis in 85 cases . Basal cell degeneration and pigment incontinence was seen in all the cases. Band-like inflammatory infiltrate was seen in the upper dermis in 90 cases.

2. Saw - Toothing of rete ridges was seen in 80 cases

3. Colloid bodies were identified in 40 cases.

4. LPP – showed perifollicular infiltrate predominantly.

5. LP pigmentosus – increased melanophages and pigment basal cell layer with sparse infiltrate in dermis was found.

7. Histopathological findings were consistent with clinical diagnosis in all but 8 cases which had features of lichenoid dermatitis.

9. PROVOCATIVE FACTORS

Provocative Factors	***No of Cases***
Dental (caries Tooth, Chr. Periodontitis	25
ENT (pharyngitis, tonsillitis DNS)	15
UTI	5

Provocative Factors	*No of Cases*
Entamoeba cysts	4
Reduced Hb%	10
Increased ESR	5
Liver function test abnormalities	Nil
HBsAg positivity	Nil

10. ASSOCIATED DISORDERS

Associated Disorder	*No of Cases*
Hypertension	4
Diabetes Mellitus	5
Psoriasis	1
Genital Vitiligo	1
Tinea capitis	1
Palmoplantar hyperhidrosis	1

DISCUSSION

1. AGE INCIDENCE

Maximum incidence of 66 % was found in the age group of 30 to 59 years. The disease was uncommon in the extremes of age. This is in contrast to various Indian studies , showing 20-39 yrs[29] and 20-49[33] yrs as the commonest age groups affected .

2. SEX INCIDENCE

Slight female preponderance[31] (F:M - 1.2:1) was found in this study.

3. SYMPTOMATOLOGY

Moderate to severe itching[31] was the predominant symptom in nearly all cases. Patients with oral lesions had burning sensation on intake of spicy foods.

4. No positive family history was found in any case similar to the study by Garg et al. The duration varied from 1 week to 4 years.

5. History of recurrence was found in 5% cases as compared to 19.3% cases in a study by Bhatacharya et al.

6. CLINICAL TYPES

Classical LP (66%) was the commonest followed by hypertrophic (2%) and linear LP (6 %).

The incidence of actinic LP was high in a few studies [33,97] but in our study only 2 case of actinic LP were seen.

The incidence of follicular LP & LP pigmentosus was less then 5% consistent with other studies [30,31]. No case of bullous LP , ulcerative LP or atrophic LP was seen in our study. No malignant transformation of hypertrophic lesions was found.

Cutaneous LP with mucosal involvement was seen in 22 cases as in studies by Garg et al; Bhatacharya et al. Isolated oral mucosal involvement was seen in 3 cases as in study by Garg et al.

Nails were involved with cutaneous LP in 10 cases (Garg et al). which is consistent with literature.

7. MORPHOLOGY AND DISTRIBUTION OF LESIONS

1. Papules and plaques were the predominant lesions found in 84 % similar to the study by Garg et al.

2. Lower limb was the initial site of involvement in 60 % as in study by Kacchawa et al.

3. Generalised cutaneous involvement was seen in 25 % cases.

4. Koebnerization was found in 30 %.

5. Hypertrophic, linear,follicular LP & LP pigmentosus showed classical features as in the literature.

6. 2 % of Zosteriform LP were described.

7. Annular LP was confined to the penis

8. Mucosal involvement – Buccal mucosa was the commonest site followed by lips

   Pigmented patches & plaques were more common than reticulate networks.

9. Among patients with palmoplantar involvement, central aspect of palms and instep of soles are the commonest sites involved. Violaceous & pigmented

plaques are commoner than yellowish plaques found in literature.

11. Longitudinal ridging was the commonest nail finding followed by longitudinal melanonychia consistent with literature.

8. HISTOPATHOLOGY

Histopathology was consistent with clinical diagnosis in all but 8 cases which showed features of lichenoid dermatitis.

9. PROVOCATIVE FACTORS

1. ENT & Dental sepsis was found in 40% but, how far, this is provocative in causing LP needs to be determined.

2. Anemia was found in 10 % & ESR raised in 5 % Garg et al study found all the blood investigations to be normal.

UTI was found in 5% and Amoebic cysts in 4%. These findings cannot be considered significant as the number of positive cases is low and similar findings

would be seen if we take 100 healthy subjects as controls.

10. ASSOCIATED DISORDERS

Even though hypertension was seen in 4 % and Diabetes in 5 %, this cannot be considered statistically significant. Studies by Kacchawa et al. & Garg etal show 1-3%association with Diabetes & hypertension.

Isolated cases of association with psoriasis, genital vitiligo, T.capitis, and palmoplantar hyperhidrosis pose no significance.

CONCLUSION

1. 30-59 years is the commonest age group affected .
2. Female preponderance in incidence was seen (1:2:1)
3. No significant positive family history
4. Mean duration – 1 week to 4 yrs. Recurrent episodes in 5%.
5. Classical LP was the commonest – 68 %
6. Papules & plaques were the commonest lesions.
7. Lower limb was the initial site of involvement
8. No malignant change was seen in hypertrophic lesions in this study
9. Oral mucosa was involved in 25%
10. Nails were involved in 10 % with longitudinal ridging being the commonest change.
11. Histopathological findings correlated with clinical findings in 92% of the cases.

12. No provocative factors could be identified statistically except for ENT and Dental sepsis which was found in 40 % of the cases.The actual significance of this finding needs to be studied further .

13. No significant association was found with any other metabolic or skin disorder.

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PROFORMA

Name :

Age/Sex : Occupation :

Address : OP. No. :

PRESENTING COMPLAINTS :

H/O PRESENT ILLNESS

Onset : Sudden / insidious

Skin lesions – Duration

Progression

Recurrence

Remission & exacerbation

Mucosal lesions – H/o dysphagia

H/o pain or burning sensation on intake of hot or spicy food

H/o itching- mild / severe

H/o photosensitivity

H/o Trauma

H/o Drug intake

H/o Focal sepsis

H/o Emotional stress

H/o dental fillings

H/o contact with photodevelopers

H/o Koebnerization

H/o sharp tooth

H/o Jaundice

H/o exposure to STD

H/o alteration in bowel & bladder habits

History suggestive of autoimmune disease (thyroiditis / vitiligo)

PAST HISTORY - H/o diabetes or Hypertension or Tuberculosis

FAMILY HISTORY - Any other family members having similar complaints

TREATMENT HISTORY - H/o treatment in the past for similar complaints

GENERAL EXAMINATION

Anemia, Jaundice, cyanosis clubbing, pedal edema, lymphadenopathy

Pulse Rate: CVS :

BP: RS :

Abdomen :

CNS :

DERMATOLOGICAL EXAMINATION

Sites affected :

Morphological type :

Wickham’s striae :

Koebnerization :

Scalp :

Palms & soles :

Mucosa : oral & genital

Nail :

Associated skin lesions – Alopecia areata, vitiligo etc

INVESTIGATIONS

1. Complete Blood Count - TC

DC

Hb%

Platelet count

2. Urine – Albumin, Sugar, Deposits

3. Motion – Ova & cyst

4. Blood VDRL

5. Random Blood Sugar

6. Liver Function test

7. HBsAg

8. Skin Biopsy